REMARKS

The pending Office Action addresses claims 1-6, all of which stand rejected. Applicants respectfully request reconsideration based on the remarks submitted herewith.

Rejections Pursuant to 35 U.S.C. § 103(a)

Claims 1-4 and 6

The Examiner rejects claims 1-4 and 6 pursuant to 35 U.S.C. § 103(a) as being obvious over U.S. Patent No. 5,437,999 of Diebold et al. ("Diebold") in view of U.S. Patent No. 5,089,320 of Straus et al. ("Straus"), U.S. Patent No. 5,095,407 of Kanezawa et al. ("Kanezawa"), a June 2001 Imaging Technologies Update from Enthone ("Enthone"), U.S. Patent No. 5,243,516 of White ("White"), and either of two articles from the Journal of Electroanalytical Chemistry, one of which is entitled "Direct Determination of Diffusion Coefficients by Chronoamperometry at Microdisk Electrodes" by Denuault et al. ("Denuault"), and the other of which is entitled "Cyclic Voltammetry for Reversible Redox-Electrode Reaction in Thin Layer Cells with Closely Separated Working and Auxiliary Electrodes of the Same Size" by Daruházi et al. ("Daruházi"). In particular the Examiner argues that the combination of Diebold, Straus, Kanezawa, Enthone, and White teaches the claimed invention except for the "means for measuring from cell current the diffusion coefficient of a redox mediator in the cell and independently its concentration." The Examiner relies on the teachings of Denuault or Daruházi to remedy the deficiencies of the combination of the other references. We respectfully disagree.

Claim 1 is directed to an apparatus for determining a concentration of glucose in a blood sample that includes a hollow electrochemical cell, means for applying an electric potential difference, means for measuring a current, and means for measuring from a cell current the diffusion coefficient of a redox mediator in the cell and independently its concentration. The hollow electrochemical cell includes at least one non-metal working electrode, at least one counter electrode or counter/reference electrode, a spacer interposed between the working electrode and the counter electrode or counter/reference electrode, and a fluid permeable side wall on at least one side of the hollow cell. The working electrode and the counter electrode or counter/reference electrode face each other, are not co-planer, and are separated by a distance of from about 20 microns to about 200 microns. The spacer includes a non-conductive polymeric material and walls of the spacer and the

electrodes define the hollow electrochemical cell. The fluid permeable side-wall permits entry of the sample into the cell and the hollow electrochemical cell has an effective cell volume of less than 1.5 microliters. The means for applying an electric potential difference applies the potential difference between the working electrode and the counter electrode or counter/reference electrode. The means for measuring a current measures current between the working electrode and the counter electrode or counter/reference electrode. No combination of Diebold, Straus, Kanezawa, Enthone, White, and Denuault or Daruházi teaches or even suggests such an apparatus.

The Examiner asserts that the teachings of Denuault or Daruházi will allow a person having ordinary skill in the art to more accurately determine the Cottrell current using the algorithm of White in the electrochemical sensor of Diebold. The Examiner states that both Denuault and Daruházi disclose means for measuring from cell current the diffusion coefficient of a redox mediator in a cell and independently its concentration. More particularly, the Examiner argues that the means of both Denuault and Daruházi allow the value of the diffusion coefficient to be actually determined, and that determining such value allows for the more accurate determination of the Cottrell current of the cell of Diebold using the algorithm of White. This argument, however, fails to account for the fact that the Cottrell current, which White relies upon, is not capable of allowing both the diffusion coefficient and the concentration of glucose to be determined independently. (*See at least* paragraph [0056] of the published application.) The Examiner's argument also fails to account for the fact that both Denuault and Daruházi teach methods that generate ***non-***Cottrell currents. A person having ordinary skill in the art would recognize that the value of the diffusion coefficient in a non-Cottrell current like the ones generated in Denuault and Daruházi is not compatible with determinations made using a Cottrell current like the one generated in White.

The Cottrell current is determined by the following equation:

$$i = \frac{nFA\sqrt{D}C_o}{\sqrt{\pi t}}$$

where:

- i is the current measured;
- n is the number of moles of electrons transferred per mole of electroactive species reacted;
- F is Faraday's Constant;
- A is the electrode area;

- D is the diffusion coefficient;
- C_O is the concentration of the electroactive species; and
- t is time.

(*See* Col. 1, line 67 to Col. 2, line 14 of White.) The present invention requires the independent determination of the diffusion coefficient (D) and the concentration of the electroactive species (C_O), which in view of the Cottrell current equation, requires that the current (i), time (t), Faraday's Constant (F), the electrode area (A), and the number of moles of electrons transferred per mole of electroactive species reacted (n) for a given electrochemical sensor be known. Even if all of these other variables are known, White provides no teachings that allow for the *independent* determination of D and C_O. A person having ordinary skill in the art would recognize that the value of D and C_O depend from each other in the Cottrell equation, and an independent determination of either is not possible with this equation. Applicants recognized the deficiencies of the Cottrell current equation from the outset, clearly stating at paragraph [0056] of the present application that "[b]y measuring the Cottrell current at known times after application of a potential to the sensor electrodes it is only possible to determine the product concentration times square root of the diffusion coefficient and therefore *it is not possible to determine the concentration of the mediator independent of its diffusion coefficient.*" (Emphasis added.) In order to remedy the deficiencies of White's reliance on the Cottrell equation, the Examiner argues that the calculations performed in either Denuault or Daruházi would suffice to determine one of these values so the other value can then be determined using the Cottrell equation. However, in order for either of these values to be compatible with the Cottrell equation, they have to be generated using a Cottrell current. Neither Denuault nor Daruházi generate a Cottrell current.

The teachings of Denuault are directed to microdisk and microsphere electrodes, ***not*** planar electrodes, i.e. the types of electrodes taught by Diebold. A person having ordinary skill in the art would recognize that the microdisk and microsphere electrodes disclosed in Denuault are actually the source of the ***non-***Cottrell behavior exhibited by its device. The calculations taught by Denuault, in fact, *require* a value for a disk radius. (*See* Abstract on page 27, stating that the method "requires only a value for the disk radius"; and the first paragraph of the INTRODUCTION on pages 27-28, stating that the method "requires only knowledge of the disk radius (a)."). More particularly, Denuault teaches that a diffusion coefficient can be determined by analyzing a microdisk chronoamperometric response when a radius of the microdisk is known. (*See* THEORY section on page 29, illustrating calculations used to determine the diffusion coefficient D, which is a function of

the radius *a* of the microdisk.) Denuault goes on to discuss a number of linear expressions for the transient, each of which is determined using the variable "*a*," i.e., the radius of the microdisk, stating that each of the equations can be used for the direct determination of the diffusion coefficient. (*See* equations 10-13 and the last paragraph on page 31.) Denuault also teaches using microsphere electrodes to determine the diffusion coefficient, but these teachings are also calculated based on a radius of the electrodes, in this case sphere radius r_s. (*See* page 32, including equation 14.) Denuault fails to provide any teachings that do not rely on the value of the radius of a microdisk or microsphere electrode. Accordingly, the teachings of Denuault, which exhibit only ***non***-Cottrell behavior, cannot be applied to the Cottrell current of White to measure from cell current the diffusion coefficient of a redox mediator in the cell and independently its concentration.

The teachings of Daruházi are directed to determining a diffusion coefficient of the substrate and *a distance between working and auxiliary electrodes* simultaneously. (*See* ABSTRACT.) The calculations relied upon in Daruházi are not applicable to a device that uses Cottrell current. This is at least because the calculations in Daruházi rely on both an enhanced current response and a steady-state current. (*See* page 78, paragraph 2.) A person having ordinary skill in the art would recognize that there can be no enhanced current response and no steady-state current achieved for a Cottrell response to occur because the Cottrell equation does not account for either an enhanced current or a steady-state current. At least because Daruházi relies on ***non***-Cottrell currents, it cannot be combined with White to arrive at the present invention.

Further, in asserting that Daruházi teaches a method for independently determining both a diffusion coefficient and a concentration of glucose, the Examiner points to the fourth paragraph on page 87. This section, however, discusses determining the value of the diffusion coefficient (D) and the value of the distance between the electrode and auxiliary electrode (δ), *not* the concentration of glucose. (*See* page 87, paragraph 4.) Daruházi teaches that the exact value of a distance between the electrode and auxiliary electrode (δ) is unknown in a clamped configuration, and then explains in the section referenced by the Examiner how δ can be determined in such a configuration. (*Id.* at paragraphs 3 and 4.) However, in order to solve for δ using the methods described by Daruházi, the value of the concentration (C_O) needs to already be known. (*See* page 81, equation 32.) In fact, there is no indication in Daruházi that the value of the concentration (C_O) is ever unknown, and there is certainly no teaching in Daruházi the shows that the diffusion coefficient (D) and *the concentration of glucose* (C_O) can be independently determined. Furthermore, to the extent that the teachings that

the Examiner relies on can subsequently be used to teach determining the concentration of glucose, such teachings cannot be said to be independent determinations because Daruházi teaches using a ratio of the distance (δ) and the diffusion coefficient (D). (*See* page 87, paragraph 4.) A ratio is inherently not an independent determination.

The teachings of both Denuault and Daruházi rely on a ***non-***Cottrell generated current, and thus are not applicable to the Cottrell current equations relied upon by the cell of Diebold in using the algorithms of White. The teachings of Denuault and Daruházi cannot be taken in a vacuum. In order for the proposed combination to work, the teachings of either Denuault or Daruházi, which rely on ***non-***Cottrell current, must be workable with the Cottrell equation taught by White. They are not. As Applicants recognized in the present application at paragraph [0056], and as a person having ordinary skill in the art would also recognize, the Cottrell equation does not allow for the independent determination of both the diffusion coefficient (D) and the concentration of glucose (C_O). Thus, the teachings of Denuault or Daruházi cannot be combined with the invention of Diebold and algorithms of White to arrive at the present invention. Such a combination would not be operable.

Accordingly, independent claim 1, as well as claims 2-4 and 6 which depend therefrom, distinguishes over Diebold in view of Straus, Kanezawa, Enthone, White, and Denuault or Daruházi and thus represents allowable subject matter.

Claim 5

The Examiner rejects claim 5 pursuant to 35 U.S.C. § 103(a) as being obvious over Diebold in view of Straus, Kanezawa, Enthone, White, and Denuault or Daruházi, further in view of U.S. Patent No. 5,126,034 of Carter et al. ("Carter") and U.S. Patent No. 5,399,256 of Bohs et al. ("Bohs").

As noted above, Diebold in view of Straus, Kanezawa, Enthone, White, and Denuault or Daruházi do not teach or even suggest an electrochemical biosensor that includes both a hollow electrochemical cell and a means for measuring from a cell current a diffusion coefficient of a redox mediator in a cell and independently its concentration as claimed by Applicants. Carter and Bohs fail to remedy the deficiencies of Diebold, Straus, Kanezawa, Enthone, White, and Denuault or Daruházi. Accordingly, at least because it is dependent upon an allowable base claim (independent claim 1), claim 5 distinguishes over Diebold in view of Straus, Kanezawa, Enthone, White, and Denuault or

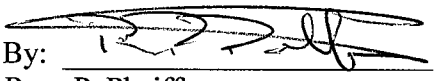
Daruházi, further in view of Carter and Bohs, and thus represents allowable subject matter.

Conclusion

In view of the reasons set forth above, each of the presently pending claims in this application is believed to be in condition for allowance, and reconsideration is respectfully requested. The Examiner is urged to telephone the undersigned Attorney for Applicants in the event that such communication is deemed to expedite prosecution of this matter.

Dated: October 24, 2008

Respectfully submitted,



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